

10/533081

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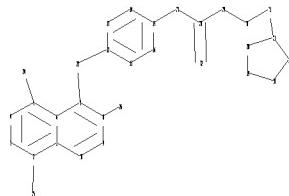
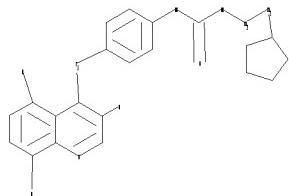
L* * * * * STN Columbus * * * * * * * * * * * *

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chain nodes :
22 24 25 26 27 28 29 30 31 32
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
chain bonds :
2-25 5-24 7-22 8-26 12-22 15-27 21-31 27-28 28-29 28-32 29-30 30-31
ring bonds :
1-2 1-6 1-10 2-3 3-4 4-5 5-6 6-7 7-8 8-9 9-10 11-12 11-16 12-13 13-14
14-15 15-16 17-18 17-21 18-19 19-20 20-21

10/533081

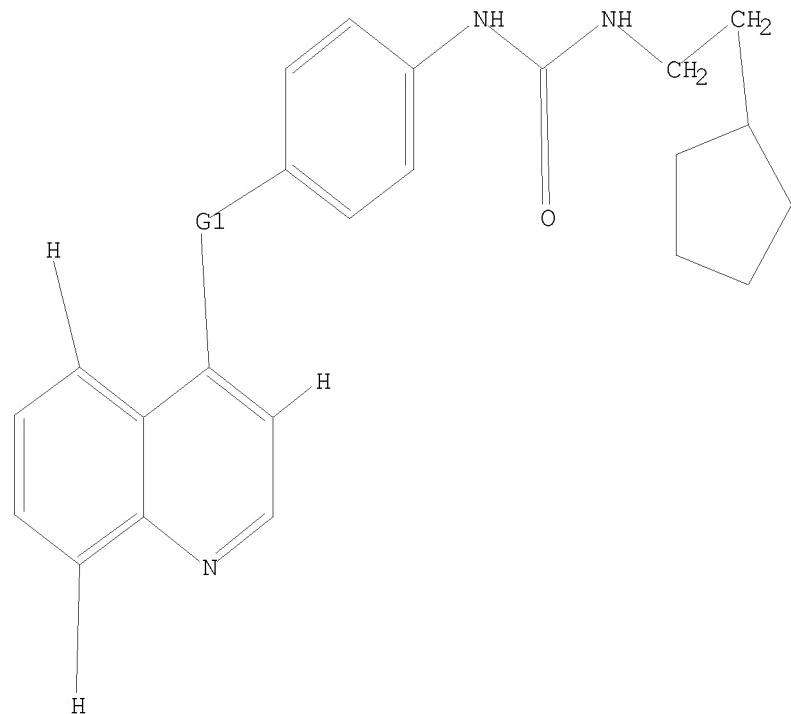
exact/norm bonds :
7-22 12-22 15-27 27-28 28-29 28-32
exact bonds :
2-25 5-24 8-26 17-18 17-21 18-19 19-20 20-21 21-31 29-30 30-31
normalized bonds :
1-2 1-6 1-10 2-3 3-4 4-5 5-6 6-7 7-8 8-9 9-10 11-12 11-16 12-13 13-14
14-15 15-16
isolated ring systems :
containing 1 : 11 : 17 :

G1:O,S

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:Atom 21:Atom 22:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS 28:CLASS
29:CLASS 30:CLASS 31:CLASS 32:CLASS

L1 STRUCTURE UPLOADED

=> d 11
L1 HAS NO ANSWERS
L1 STR



G1 O,S

Structure attributes must be viewed using STN Express query preparation.

10/533081

=> s 11 sam
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SAMPLE SCREEN SEARCH COMPLETED - 19 TO ITERATE

100.0% PROCESSED 19 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 119 TO 641
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s 11 full
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L4 1 L3

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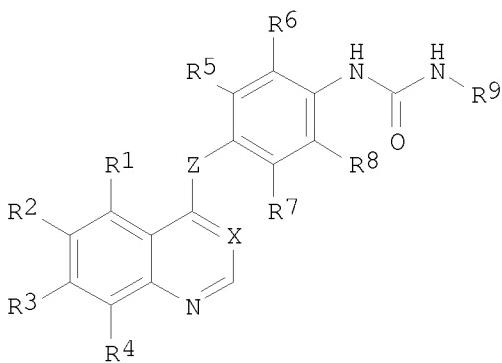
L4 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:390229 CAPLUS
DOCUMENT NUMBER: 140:406748
TITLE: Preparation of quinoline derivatives and quinazoline derivatives inhibiting autophosphorylation of Flt3 and medicinal compositions containing the same
INVENTOR(S): Hirai, Hisamaru; Miwa, Atsushi; Yoshino, Tetsuya;
Kurokawa, Mineo
PATENT ASSIGNEE(S): Kirin Beer Kabushiki Kaisha, Japan; Hirai, Naoko
SOURCE: PCT Int. Appl., 118 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2004039782	A1	20040513	WO 2003-JP13848	20031029
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
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 AU 2003280599 A1 20040525 AU 2003-280599 20031029
 EP 1566379 A1 20050824 EP 2003-769958 20031029
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
 US 20080207617 A1 20080828 US 2006-533081 20061109
 PRIORITY APPLN. INFO.: JP 2002-314670 A 20021029
 WO 2003-JP13848 W 20031029

OTHER SOURCE(S): MARPAT 140:406748

GI



AB Disclosed is a medicinal composition to be used in preventing or treating diseases which can be effectively treated or prevented by inhibiting autophosphorylation of Flt3, comprising a compound represented by the following general formula (I) or pharmaceutically acceptable salts thereof or solvates of the same [wherein X = CH, N; Z = O, S; R1, R2, R3 = H, OH, halo, NO₂, cyano, CHO, or each optionally substituted NH₂, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C1-6 alkoxy, C1-4 alkyl-carbonyl, or CONH₂; R4 = H; R5 = R6 = R7 = R8 = H, or 1 or 2 number of R5-R8 = halo, C1-4 alkyl, C1-4 alkoxy, NO₂, NH₂, OH and all the others = H; R9 = (a) saturated 3- to 9-membered carbocyclyl optionally substituted by 1-3 number of C1-4 alkyl or (b) C1-4 alkyl substituted by C1-4 alkoxy, 5- or 6-membered heterocyclyl, each (un)substituted saturated 3- to 9-membered carbocyclyl, iso-Pr, tert-Bu, or NH₂]. The diseases which can be effectively treated by inhibiting autophosphorylation of Flt3 include hematopoietic malignant tumor, in particular acute myelocytic leukemia or bone marrow neoplastic abnormality syndrome. Thus, 2 g 4-[(6,7-dimethoxy-4-quinolinyl)oxy]aniline was dissolved in 100 mL CHCl₃, treated dropwise with a solution of 2 mL Et₃N and 1 g triphosgene in 4 mL CHCl₃, stirred at room temperature for 30 min, treated with 750 mg 3,3-dimethylbutylamine, and stirred at room temperature for 5 h to give, after workup and silica gel chromatog., N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]phenyl]-N'-(3,3-dimethylbutyl)urea (II). II.HCl and N-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]-3-fluorophenyl]-N'-(3,3-dimethylbutyl)urea hydrochloride showed IC₅₀ of 2 and <1 nM, resp., for inhibiting the autophosphorylation of MV4-11 human leukemia cell.

IT 688309-27-5P 688309-49-1P 688309-61-7P

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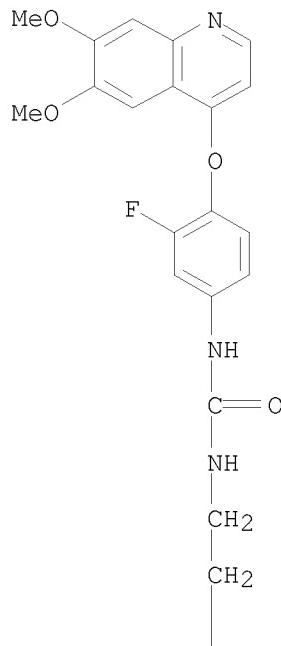
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of quinoline and quinazoline derivs. as inhibitors of autophosphorylation of FMS-like tyrosine kinase 3 (Flt3) for treatment or preparation of hematopoietic malignant tumor)

RN 688309-27-5 CAPLUS

CN Urea, N-(2-cyclopentylethyl)-N'-[4-[(6,7-dimethoxy-4-quinolinyl)oxy]-3-fluorophenyl]- (CA INDEX NAME)

PAGE 1-A



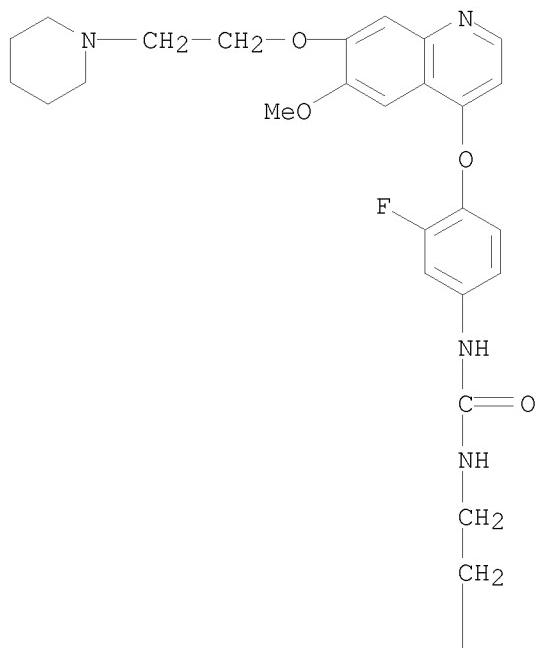
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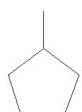
RN 688309-49-1 CAPLUS

CN Urea, N-(2-cyclopentylethyl)-N'-[3-fluoro-4-[[6-methoxy-7-[2-(1-piperidinyl)ethoxy]-4-quinolinyl]oxy]phenyl]- (CA INDEX NAME)

PAGE 1-A



PAGE 2-A

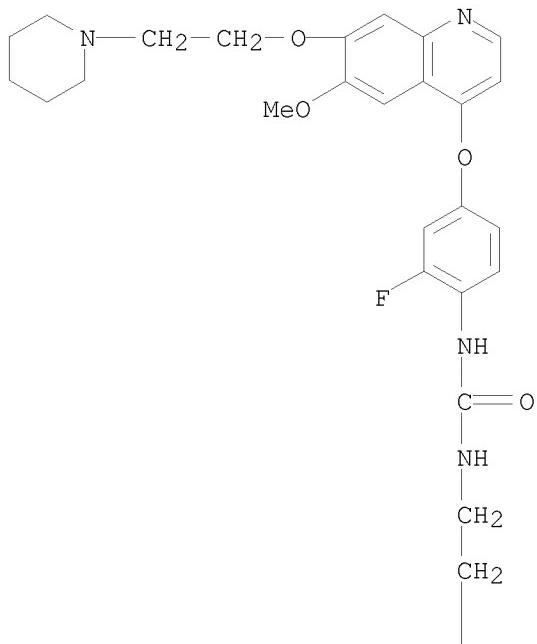


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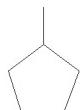
CN Urea, N-(2-cyclopentylethyl)-N'-[2-fluoro-4-[[6-methoxy-7-[2-(1-piperidinyl)ethoxy]-4-quinolinyl]oxy]phenyl]- (CA INDEX NAME)

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PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> file marpat

=> s 13 full
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FULL SCREEN SEARCH COMPLETED - 6395 TO ITERATE

100.0% PROCESSED 6395 ITERATIONS
SEARCH TIME: 00.00.05

2 ANSWERS

L5 2 SEA SSS FUL L1

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10/533081

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L1 STRUCTURE uploaded

L2 0 S L1 SAM

L3 3 S L1 FULL

FILE 'CAPLUS' ENTERED AT 14:20:10 ON 01 JUL 2009

L4 1 S L3

FILE 'MARPAT' ENTERED AT 14:20:19 ON 01 JUL 2009

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L5 ANSWER 1 OF 2 MARPAT COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 140:406748 MARPAT

TITLE: Preparation of quinoline derivatives and quinazoline derivatives inhibiting autophosphorylation of Flt3 and medicinal compositions containing the same

INVENTOR(S): Hirai, Hisamaru; Miwa, Atsushi; Yoshino, Tetsuya; Kurokawa, Mineo

PATENT ASSIGNEE(S): Kirin Beer Kabushiki Kaisha, Japan; Hirai, Naoko

SOURCE: PCT Int. Appl., 118 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

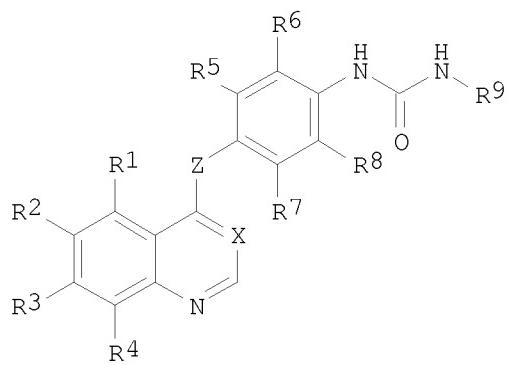
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

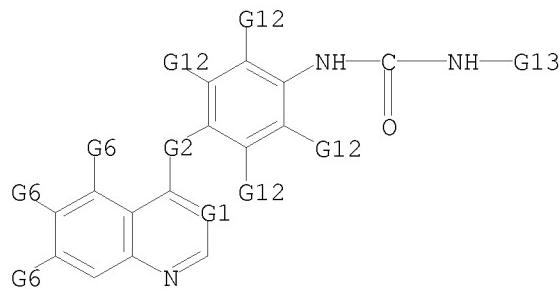
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AU 2003280599	A1	20040525	AU 2003-280599	20031029
EP 1566379	A1	20050824	EP 2003-769958	20031029
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 20080207617	A1	20080828	US 2006-533081	20061109
PRIORITY APPLN. INFO.:			JP 2002-314670	20021029
			WO 2003-JP13848	20031029

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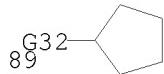


AB Disclosed is a medicinal composition to be used in preventing or treating diseases which can be effectively treated or prevented by inhibiting autophosphorylation of Flt3, comprising a compound represented by the following general formula (I) or pharmaceutically acceptable salts thereof or solvates of the same [wherein X = CH, N; Z = O, S; R1, R2, R3 = H, OH, halo, NO₂, cyano, CHO, or each optionally substituted NH₂, C1-6 alkyl, C2-6 alkenyl, C2-6 alkynyl, C1-6 alkoxy, C1-4 alkyl-carbonyl, or CONH₂; R4 = H; R5 = R6 = R7 = R8 = H, or 1 or 2 number of R5-R8 = halo, C1-4 alkyl, C1-4 alkoxy, NO₂, NH₂, OH and all the others = H; R9 = (a) saturated 3- to 9-membered carbocyclyl optionally substituted by 1-3 number of C1-4 alkyl or (b) C1-4 alkyl substituted by C1-4 alkoxy, 5- or 6-membered heterocyclyl, each (un)substituted saturated 3- to 9-membered carbocyclyl, iso-Pr, tert-Bu, or NH₂]. The diseases which can be effectively treated by inhibiting autophosphorylation of Flt3 include hematopoietic malignant tumor, in particular acute myelocytic leukemia or bone marrow neoplastic abnormality syndrome. Thus, 2 g 4-[(6,7-dimethoxy-4-quinolinyl)oxygen]aniline was dissolved in 100 mL CHCl₃, treated dropwise with a solution of 2 mL Et₃N and 1 g triphosgene in 4 mL CHCl₃, stirred at room temperature for 30 min, treated with 750 mg 3,3-dimethylbutylamine, and stirred at room temperature for 5 h to give, after workup and silica gel chromatog., N-[4-[(6,7-dimethoxy-4-quinolinyl)oxygen]phenyl]-N'-(3,3-dimethylbutyl)urea (II). II.HCl and N-[4-[(6,7-dimethoxy-4-quinolinyl)oxygen]-3-fluorophenyl]-N'-(3,3-dimethylbutyl)urea hydrochloride showed IC₅₀ of 2 and <1 nM, resp., for inhibiting the autophosphorylation of MV4-11 human leukemia cell.

MSTR 1



G1 = CH
 G2 = O
 G13 = 89



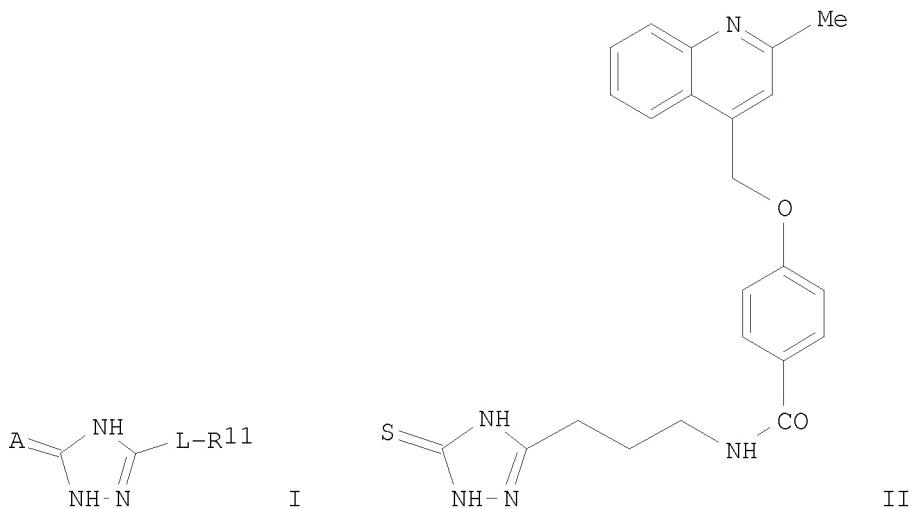
G32 = (2-4) CH₂
 Patent location: claim 1
 Note: or pharmaceutically acceptable salts or solvates
 Note: additional ring formation also claimed

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 2 MARPAT COPYRIGHT 2009 ACS on STN
 ACCESSION NUMBER: 140:357353 MARPAT
 TITLE: Preparation of triazolone and triazolethione inhibitors of matrix metalloproteinases and/or TNF- α converting enzyme as anti-inflammatory agents
 INVENTOR(S): King, Bryan W.; Sheppeck, James; Gilmore, John L.
 PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
 SOURCE: PCT Int. Appl., 125 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

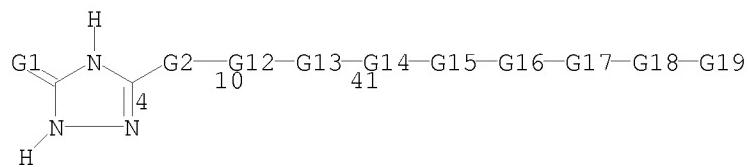
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004032846	A2	20040422	WO 2003-US31537	20031003
WO 2004032846	A3	20040715		
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US 20040116491	A1	20040617	US 2003-678331	20031003
US 7074810	B2	20060711		
EP 1558581	A2	20050803	EP 2003-776228	20031003
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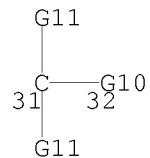


AB The present application describes novel hydantoin derivs. (shown as I; A = O, S; L-R11 represents a very large variety of substituents and is defined in the claims; e.g. II) or pharmaceutically acceptable salt or prodrug forms thereof, which are useful as inhibitors of matrix metalloproteinases (MMP), TNF- α converting enzyme (TACE), aggrecanase, or a combination thereof. Some examples of I exhibit Ki's <10 μ M but individual data are not presented. Although the methods of preparation are not claimed, 37 example preps. are included. For example, II was prepared in 4 steps (100, 66, 73 and 82%, resp.) starting with condensation of Et 4-aminobutyrate hydrochloride with 4-(2-methylquinolin-4-ylmethoxy)benzoyl chloride hydrochloride followed by base hydrolysis to the acid, followed by hydrazide formation with thiosemicarbazide followed by cyclization.

MSTR 1



$$G_2 = 31-4 \quad 32-10$$



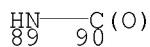
10/533081

G10 = 108



G12 = carbon chain <containing 1 or more C,
0 or more double bonds, 0 or more triple bonds>
(opt. substd.)

G13 = 89-10 90-41



G14 = bond
G15 = NH (opt. substd.)
G16 = phenylene (opt. substd.)
G17 = O
G18 = bond
G19 = quinolinyl (opt. substd. by G23)

Patent location: claim 1

Note: or pharmaceutically acceptable salts

Note: additional ring formation also claimed

Note: substitution is restricted

Stereochemistry: or stereoisomers

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE 'REGISTRY' ENTERED AT 14:19:45 ON 01 JUL 2009

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L5 2 S L3 FULL

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